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I U C L I D

Data Set

Existing Chemical : ID: 84-75-3
CAS No. : 84-75-3
EINECS Name : Dihexyl phthalate
Molecular Weight : 334.5
Molecular Formula : C₂₀H₃₀O₄

Producer related part
Company : ExxonMobil Biomedical Sciences Inc.
Creation date : 07.11.2000

Substance related part
Company : ExxonMobil Biomedical Sciences Inc.
Creation date : 07.11.2000

Status :
Memo : ACC Phthalate Esters Panel HPV Testing group

Printing date : 05.12.2006
Revision date :
Date of last update : 05.12.2006

Number of pages : 27

Chapter (profile) : Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile) : Reliability: without reliability, 1, 2, 3, 4
Flags (profile) : Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE),
Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1. General Information

Id 84-75-3

Date 05.12.2006

1.0.1 APPLICANT AND COMPANY INFORMATION

Type : lead organisation
Name : ACC Phthalate Esters Panel HPV Testing Group
Contact person : Dr. Marian Stanley
Date :
Street : 1300 Wilson Blvd.
Town : 22209 Arlington, VA
Country : United States
Phone : (703) 741-5623
Telefax : (703) 741-6091
Telex :
Cedex :
Email :
Homepage :

Remark : The American Chemistry Council Phthalate Esters Panel includes the following member companies:

BASF Corporation
CONDEA Vista Company
Eastman Chemical Company
ExxonMobil Chemical Company
Ferro Corporation
ICI Americas / Uniqema
Sunoco Chemicals
Teknor Apex Company

27.04.2006

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

Comment : This chemical is not a member of the Transitional Phthalate Esters subcategory but its data are being used to support a hazard assessment of the subcategory.

Remark : This chemical is not a member of the Transitional Phthalate Esters subcategory but its data are being used to support a hazard assessment of the subcategory. The Transitional Phthalate Esters subcategory includes the following six CAS numbers and names:
68515-50-4 1,2,-benzenedicarboxylic acid, dihexyl ester, branched and linear (DHP)
71888-89-6 1,2-benzenedicarboxylic acid, di C6-8 branched alkyl ester, C7 rich (DIHP)
27554-26-3 1,2,-benzenedicarboxylic acid, diisooctyl ester (DIOP)
68515-44-6 1,2-benzenedicarboxylic acid, diheptyl ester, branched and linear (DinHP)
111381-89-6 1,2-benzenedicarboxylic acid (C7, C9) ester, branched and linear (79P)
111381-90-9 1,2-benzenedicarboxylic acid, (C7,C11) ester, branched and linear (711P)

The phthalate esters comprise a family of chemicals synthesized by esterifying phthalic anhydride with various alcohols in the presence of an acid catalyst. Phthalate esters are all 1,2-benzenedicarboxylic acids with side chain ester groups ranging from C1 to approximately C13. The structural characteristics of the ester side chains affect both the physical/chemical and biological properties of phthalate esters.

Phthalate esters are generally clear to yellow, oily liquids with high boiling ranges (>250°C) and low vapor pressures; properties which contribute to their high physical stability. They are readily soluble in most organic solvents and miscible with alcohol, ether and most oils. The aqueous solubility of phthalate esters is inversely related to their molecular weights. Lower molecular weight phthalates exhibit slight to moderate water solubility, whereas, higher molecular weight phthalates are insoluble.

The phthalate esters were subdivided into three subcategories based on their physicochemical and toxicological properties. The phthalate esters in this subcategory, Transitional phthalates, are produced from alcohols with straight-chain carbon backbones of C4-6. Phthalate esters containing >10% C4-6 molecules were conservatively included in this subcategory. Six of the U.S. HPV chemicals, dihexyl (DHP), diheptyl, diisooheptyl, diisooctyl, heptyl nonyl (C7, C9) and heptyl undecyl (C7, C11) phthalates are included in this subcategory. Data for this subcategory were supplemented with published information on other phthalate esters currently being assessed under the OECD SIDS program, including dibutyl (DBP), butylbenzyl (BBP), and di(2-ethylhexyl) phthalate (DEHP). Data on a structurally similar material, di-n hexyl phthalate, was also included for read-across purposes.

Transitional phthalates have varied uses from solvents (e.g., dibutyl) to plasticizers for PVC (e.g., DEHP). Physicochemical properties also vary in that the lower molecular weight transitional phthalates are more water-soluble than higher transitional phthalates, but none would be considered to fall into the "high water soluble" category. What distinguishes these phthalates from others is their greater mammalian toxicity potential, particularly with regard to reproductive and developmental effects, compared to either the low or high molecular weight phthalate subcategories. Of the phthalates in this subcategory, DEHP appears to be the most potent for liver and reproductive/developmental endpoints.

27.04.2006

1.1.0 SUBSTANCE IDENTIFICATION

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	
Substance type	:	organic
Physical status	:	liquid
Purity	:	% w/w
Colour	:	
Odour	:	

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1.1.2 SPECTRA

1. General Information

Id 84-75-3
Date 05.12.2006

1.2 SYNONYMS AND TRADE NAMES

1.3 IMPURITIES

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : industrial
Category : Polymers industry

Remark : Transitional phthalates have varied uses from solvents (e.g., dibutyl) to plasticizers for PVC (e.g., DEHP).

27.04.2006

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1. General Information

Id 84-75-3
Date 05.12.2006

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2. Physico-Chemical Data

Id 84-75-3
Date 05.12.2006

2.1 MELTING POINT

Value : -27 °C
Decomposition : no, at °C
Sublimation :
Method : other: no data
Year :
GLP :
Test substance : other TS: CAS #84-75-3; dihexyl phthalate

Remark : Data are from a peer reviewed literature review of data from a variety of sources including manufacturer's data or handbook values.
Test substance : CAS #84-75-3; dihexyl phthalate
Reliability : (2) valid with restrictions
This robust summary is assigned a reliability of 2 because there is limited information on how the data were developed.

Flag : Critical study for SIDS endpoint
05.04.2006

(8)

Value : 48 °C
Decomposition : no, at °C
Sublimation : no
Method :
Year :
GLP :
Test substance : other TS: CAS #84-75-3; dihexyl phthalate

Method : Melting point calculation by MPBPWIN ver. 1.41 using calculation methods of Joback and Gold and Ogle.

Remark : EPI Suite™ is used and advocated by the US EPA for chemical property estimation. However, the melting point calculation in EPI Suite™ gives erroneously high results for the phthalate esters.

Test substance : CAS #84-75-3; dihexyl phthalate
Reliability : (3) invalid

05.12.2006

(2)

2.2 BOILING POINT

Value : 385 °C at 1013 hPa
Decomposition : no
Method : other: calculation
Year :
GLP :
Test substance : other TS: CAS #84-75-3; dihexyl phthalate

Method : Boiling point calculation by MPBPWIN ver. 1.41 using calculation method of Stein and Brown.

Remark : EPI Suite™ is used and advocated by the US EPA for chemical property estimation.

Test substance : CAS #84-75-3; dihexyl phthalate
Reliability : (2) valid with restrictions

This robust summary has a reliability rating of 2 because the data are calculated.

Flag : Critical study for SIDS endpoint
05.04.2006

(2)

2.3 DENSITY

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = .00000345 hPa at °C

Decomposition : no

Method : other (calculated)

Year :

GLP :

Test substance : other TS: CAS #84-75-3; dihexyl phthalate

Method : Measured data collected and tabulated, calculated data also considered in determining recommended values.

Remark : Physicochemical data for selected commercial phthalate esters from various sources including the public literature, manufacturing specifications, and handbook values were evaluated by an industry peer review process. Valid values were identified and presented in a phthalate ester environmental fate, peer reviewed publication. These data, including the values for vapour pressure, represent the definitive and currently accepted physicochemical database for selected phthalate esters including dihexyl phthalate.

Quantitative structure-property relationships, significant at the 99.9% level, were developed using the relevant phthalate ester data to estimate solubility in water, air, and octanol, where V = the Le Bas molar volume (cm³ mol⁻¹). The Le Bas molar volume used for dihexyl phthalate ester was 431.6 cm³ mol⁻¹.

Log CS(WL) = -0.012V + 5.8, n = 35 (solubility in water)
r² = 0.98, SE = 0.39

Log CS(AL) = -0.013V - 1.3, n = 15 (solubility in air)
r² = 0.87, SE = 0.33

Log CS(OL) = -0.016V + 3.4, n = 68 (solubility in octanol)
r² = 0.19, SE = 0.41

It was recommended by the authors that the above regressions be used for predicting the three solubilities for phthalate esters with alkyl chain lengths from 1 to 13 carbons.

Test substance : CAS #84-75-3; dihexyl phthalate

Reliability : (2) valid with restrictions

The value was calculated based on the QSPR (quantitative structure-property relationship) three-solubility model. This robust summary has a reliability rating of 2 because the data are calculated and not measured.

Flag : Critical study for SIDS endpoint

05.04.2006

(1)

Value : .0000263 hPa at 25 °C

Decomposition : no

Method : other (calculated)

Year :

GLP :

Test substance : other TS: CAS #84-75-3; dihexyl phthalate

2. Physico-Chemical Data

Id 84-75-3

Date 05.12.2006

Method : Vapor pressure calculation by MPBPWIN ver. 1.41 using calculation method of Grain.
Remark : EPI SuiteTM is used and advocated by the US EPA for chemical property estimation.
Test substance : CAS #84-75-3; dihexyl phthalate
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.

05.04.2006 (2)

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : = 6 at 25 °C
pH value :
Method : other (calculated)
Year :
GLP :
Test substance : other TS: CAS #84-75-3; dihexyl phthalate

Method : Measured data collected and tabulated, calculated data also considered in determining recommended values.
Remark : Physicochemical data for selected commercial phthalate esters from various sources including the public literature, manufacturing specifications, and handbook values were evaluated by an industry peer review process. Valid values were identified and presented in a phthalate ester environmental fate, peer reviewed publication. These data, including the values for partition coefficient, represent the definitive and currently accepted physicochemical database for selected phthalate esters including dihexyl phthalate.

Quantitative structure-property relationships, significant at the 99.9% level, were developed using the relevant phthalate ester data to estimate solubility in water, air, and octanol, where V = the Le Bas molar volume ($\text{cm}^3 \text{mol}^{-1}$). The Le Bas molar volume used for dihexyl phthalate ester was $431.6 \text{ cm}^3 \text{mol}^{-1}$.

$\text{Log CS(WL)} = -0.012V + 5.8$, $n = 35$ (solubility in water)
 $r^2 = 0.98$, $\text{SE} = 0.39$

$\text{Log CS(AL)} = -0.013V - 1.3$, $n = 15$ (solubility in air)
 $r^2 = 0.87$, $\text{SE} = 0.33$

$\text{Log CS(OL)} = -0.016V + 3.4$, $n = 68$ (solubility in octanol)
 $r^2 = 0.19$, $\text{SE} = 0.41$

It was recommended by the authors that the above regressions be used for predicting the three solubilities for phthalate esters with alkyl chain lengths from 1 to 13 carbons.

Test substance : CAS #84-75-3; dihexyl phthalate
Reliability : (2) valid with restrictions
The value was calculated based on the QSPR (quantitative structure-property relationship) three-solubility model. This robust summary has a reliability rating of 2 because the data are calculated and not measured.

Flag : Critical study for SIDS endpoint
05.04.2006 (1)

Partition coefficient : octanol-water
Log pow : 6.6 at 25 °C
pH value :

2. Physico-Chemical Data

Id 84-75-3

Date 05.12.2006

Method : other (calculated)
Year :
GLP :
Test substance : other TS: CAS #84-75-3; dihexyl phthalate

Method : Partition coefficient by LOGKOWWIN ver. 1.67 using an atom/fragment calculation method of Meylan and Howard.
Remark : EPI Suite™ is used and advocated by the US EPA for chemical property estimation.
Test substance : CAS #84-75-3; dihexyl phthalate
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.

05.04.2006

(2)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water
Value : .159 mg/l at 25 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method : other: calculated
Year :
GLP :
Test substance : other TS: CAS #84-75-3; dihexyl phthalate

Method : Measured data collected and tabulated, calculated data also considered in determining recommended values.

Remark : Physicochemical data for selected commercial phthalate esters from various sources including the public literature, manufacturing specifications, and handbook values were evaluated by an industry peer review process. Valid values were identified and presented in a phthalate ester environmental fate, peer reviewed publication. These data, including the values for water solubility, represent the definitive and currently accepted physicochemical database for selected phthalate esters including dihexyl phthalate.

Quantitative structure-property relationships, significant at the 99.9% level, were developed using the relevant phthalate ester data to estimate solubility in water, air, and octanol, where V = the Le Bas molar volume ($\text{cm}^3 \text{mol}^{-1}$). The Le Bas molar volume used for dihexyl phthalate ester was $431.6 \text{ cm}^3 \text{mol}^{-1}$.

$\text{Log CS(WL)} = -0.012V + 5.8$, $n = 35$ (solubility in water)
 $r^2 = 0.98$, $\text{SE} = 0.39$

$\text{Log CS(AL)} = -0.013V - 1.3$, $n = 15$ (solubility in air)
 $r^2 = 0.87$, $\text{SE} = 0.33$

$\text{Log CS(OL)} = -0.016V + 3.4$, $n = 68$ (solubility in octanol)
 $r^2 = 0.19$, $\text{SE} = 0.41$

It was recommended by the authors that the above regressions be used for predicting the three solubilities for phthalate esters with alkyl chain lengths

2. Physico-Chemical Data

Id 84-75-3
Date 05.12.2006

Test substance : from 1 to 13 carbons.
Reliability : CAS #84-75-3; dihexyl phthalate
: (2) valid with restrictions
The value was calculated based on the QSPR (quantitative structure-property relationship) three-solubility model. This robust summary has a reliability rating of 2 because the data are calculated and not measured.

Flag : Critical study for SIDS endpoint
05.04.2006 (1)

Solubility in : Water
Value : = .0115 mg/l at 25 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method : other: calculated
Year :
GLP :
Test substance : other TS: CAS #84-75-3; dihexyl phthalate

Method : Water solubility calculated using WSKOWN ver 1.41 based on Kow correlation method of Meylan and Howard. Kow used in calculation was 6.82.

Remark : EPI Suite™ is used and advocated by the US EPA for chemical property estimation.

Test substance : CAS #84-75-3; dihexyl phthalate
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.

05.04.2006 (2)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2. Physico-Chemical Data

Id 84-75-3
Date 05.12.2006

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	: air
Light source	: Sun light
Light spectrum	: nm
Relative intensity	: 1 based on intensity of sunlight
Conc. of substance	: at 25 °C
INDIRECT PHOTOLYSIS	
Sensitizer	: OH
Conc. of sensitizer	: 1500000 molecule/cm ³
Rate constant	: = .0000000001493 cm ³ /((molecule*sec)
Degradation	: 50 % after 8.6 hour(s)
Deg. product	: not measured
Method	: other (calculated)
Year	:
GLP	:
Test substance	: other TS: CAS #84-75-3; dihexyl phthalate
Method	: Photodegradation rate calculated by AOPWIN ver. 1.91 based on the methods of Atkinson.
Remark	: 50% degradation after 8.6 hrs or 0.716 days based on a 12-hour day. The computer program AOPWIN (atmospheric oxidation program for Microsoft Windows) (EPI SuiteTM, 2000) calculates a chemical half-life for a 12-hour day (the 12-hour day half-life value normalizes degradation to a standard day light period during which hydroxyl radicals needed for degradation are generated), based on an OH- reaction rate constant and a defined OH- concentration. EPI SuiteTM is used and advocated by the US EPA for chemical property estimation.
Test substance	: CAS #84-75-3; dihexyl phthalate
Reliability	: (2) valid with restrictions This robust summary has a reliability rating of 2 because the data are calculated.
Flag	: Critical study for SIDS endpoint
05.07.2006	(2)

3.1.2 STABILITY IN WATER

Type	: abiotic
t1/2 pH4	: at °C
t1/2 pH7	: = 3.4 year at 25 °C
t1/2 pH9	: at °C
Deg. product	:
Method	: other (calculated)
Year	:
GLP	:
Test substance	: other TS: CAS #84-75-3; dihexyl phthalate
Method	: Hydrolysis rate calculated by HYDROWIN ver. 1.67 based on workd for EPA by T. Mill et al.
Remark	: EPI SuiteTM is used and advocated by the US EPA for chemical property estimation
Test substance	: CAS #84-75-3; dihexyl phthalate
Reliability	: (2) valid with restrictions This robust summary has a reliability rating of 2 because the data are calculated.
Flag	: Critical study for SIDS endpoint

3. Environmental Fate and Pathways

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(2)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

3.3.2 DISTRIBUTION

Media : air - biota - sediment(s) - soil - water
Method : Calculation according Mackay, Level I
Year :

Remark : Physicochemical data used in the calculation:

Parameter	Value w/ Units
-----------	----------------

Molecular Weight	334.46
Temperature	25° C
Log Kow	6.0
Water Solubility	0.159 g/m3
Vapor Pressure	.000345 Pa
Melting Point	-27°C

Result : Using the Mackay Level I calculation, the following distribution is predicted for dihexyl phthalate:

% Distribution	Compartment
0.0	Air
0.1	Water
97.6	Soil
2.2	Sediment
0.1	Suspended Sediment
0.0	Biota

Test substance : CAS #84-75-3; dihexyl phthalate
Reliability : (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.

Flag : Critical study for SIDS endpoint

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(6)

Media : air - biota - sediment(s) - soil - water
Method : Calculation according Mackay, Level III
Year :

Remark : Physicochemical data used in the calculation:

Parameter	Value w/ Units
-----------	----------------

Molecular Weight	334.46
Temperature	25° C
Log Kow	6.0

3. Environmental Fate and Pathways

Id 84-75-3
Date 05.12.2006

Water Solubility 0.159 g/m3
Vapor Pressure .000345 Pa
Melting Point -27°C

Emissions rates used in the calculation:

Compartment Rate (kg/hr)

Air 1000
Water 1000
Soil 1000

Half-lives used in the calculation:

Compartment Half-life (hr)

Air 17.2a
Water 120b
Soil 420c
Sediment 420c

a - as calculated using AOPWIN version 1.91, a subroutine of the computer program EPI Suite™ version 3.12 and normalized to a 24 hour day [Environmental Protection Agency (EPA) (2000). EPI Suite™, Estimation Program Interface Suite, v3.12. U.S. EPA, Washington, DC, USA.]

b - based on read-across biodegradation data from: Exxon Biomedical Sciences, Inc. Ready Biodegradability: Manometric Respirometry Test, Study Number 142994A, 1997 Exxon Biomedical Sciences, Inc.

Boethling R (2000). HPVC-Screening Tool: Using Ready and Inherent Biodegradability Data to Derive Input Data for the EQC Model, Appendix 10 in Environment Canada, Environmental Categorization for Persistence Bioaccumulation and Inherent Toxicity of Substances on the Domestic Substance List Using QSARs, Results of an international workshop hosted by Chemicals Evaluation Division of Environment Canada, Nov. 11-12, 1999, in Philadelphia, PA, USA.

c - based on Boethling, R. recommendation that half-lives of 3 to 4 times longer than surface water should be used for soil and sediment.

Result

- : Using the Mackay Level III calculation, the following distribution is predicted for dihexyl phthalate:

Compartment % Distribution
Air 1.8
Water 12.5
Soil 72.0
Sediment 13.7

Test substance Reliability

- : CAS #84-75-3; dihexyl phthalate
: (2) valid with restrictions
This robust summary has a reliability rating of 2 because the data are calculated.

Flag
12.05.2006

- : Critical study for SIDS endpoint

(6)

3.4 MODE OF DEGRADATION IN ACTUAL USE

3. Environmental Fate and Pathways

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3.5 BIODEGRADATION

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

- 4.1 ACUTE/PROLONGED TOXICITY TO FISH
- 4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES
- 4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE
- 4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA
- 4.5.1 CHRONIC TOXICITY TO FISH
- 4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES
- 4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS
- 4.6.2 TOXICITY TO TERRESTRIAL PLANTS
- 4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS
- 4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES
- 4.7 BIOLOGICAL EFFECTS MONITORING
- 4.8 BIOTRANSFORMATION AND KINETICS
- 4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION**5.1.1 ACUTE ORAL TOXICITY**

Type : LD50
Value : = 29.6 - ml/kg bw
Species : rat
Strain :
Sex : male/female
Number of animals :
Vehicle : no data
Doses :
Method : other
Year : 1973
GLP : no
Test substance : other TS: CAS #84-75-3; 1,2-benzenedicarboxylic acid, dihexyl ester

Result : LD50 = 29.6 ml/kg (males); 38.9 ml/kg (females).
Test substance : 1,2-benzenedicarboxylic acid, dihexyl ester (di-n-hexyl phthalate)
Conclusion : The acute oral LD50 was reported as 29.6 ml/kg (males) and 38.9 ml/kg (females).
Reliability : (4) not assignable
No experimental detail presented; LD50 values reported from unpublished sources.
Flag : Critical study for SIDS endpoint
05.12.2006 (4)

5.1.2 ACUTE INHALATION TOXICITY**5.1.3 ACUTE DERMAL TOXICITY****5.1.4 ACUTE TOXICITY, OTHER ROUTES****5.2.1 SKIN IRRITATION****5.2.2 EYE IRRITATION****5.3 SENSITIZATION****5.4 REPEATED DOSE TOXICITY**

Type :
Species : rat
Sex : male
Strain : Wistar
Route of admin. : oral feed
Exposure period : 21 Days

5. Toxicity

Id 84-75-3

Date 05.12.2006

Frequency of treatm. : Daily
Post exposure period : None
Doses : 0, 2.0% (20 g/kg in diet, estimated 1800 mg/kg/day).
Control group : yes
Method :
Year : 1985
GLP : no data
Test substance : other TS: CAS #84-75-3; 1,2-benzenedicarboxylic acid, dihexyl ester

Remark : There was no effect on food consumption or body weight gain. Liver weights were statistically increased at the terminal sacrifice (21 days). Light microscopy of the livers of the treated animals after 10 and 21 days revealed centrilobular accumulation of fat associated with some necrosis. Examination via electron microscopy showed accumulation of small lipid droplets in hepatocytes after 10 days and progression to larger droplets after 21 days. There was also some evidence of a small increase in peroxisome number. There were no biologically significant changes in liver enzymes or other biochemical analyses.

Result : NOAEL not determined.
Test condition : Following a one week acclimation period, the test or control diets were given to the rats for 21 days. The animals were observed daily and food consumption measured twice weekly. Subgroups of 4 rats were sacrificed at 3, 10 and 21 days. Liver, testes, epididymis, and seminal vesicles were weighed. Liver, kidneys, spleen, testes, epididymis, and seminal vesicles were preserved for microscopic examination. A portion of the liver also was used for enzyme and biochemical determinations

Test substance : 1,2-benzenedicarboxylic acid, dihexyl ester (di-n-hexyl phthalate)
Conclusion : Diets containing a high concentration of DnHP induced accumulation of large droplets of fat in liver centrilobular regions with mild necrosis. There were increased liver weights and evidence of a slight induction of peroxisomes, but no significant changes in any other parameters.

Reliability : (2) valid with restrictions
Screening study with single dose level and limited number of animals.

Flag : Critical study for SIDS endpoint
05.12.2006 (7)

5.5 GENETIC TOXICITY 'IN VITRO'

Type : Ames test
System of testing : Bacterial
Test concentration : 5 dose levels up to 10 mg/plate.
Cytotoxic concentr. :
Metabolic activation : with and without
Result : negative
Method : OECD Guide-line 471
Year : 1985
GLP : no data
Test substance : other TS: CAS #84-75-3; 1,2-benzenedicarboxylic acid, dihexyl ester

Method : Statistical Methods: A mutagenic response was defined as a reproducible, dose-related increase in the number of histidine-independent colonies over the spontaneous incidence. There was no requirement for a specific magnitude of increase.

Result : The test substance was negative in all strains.
Test condition : Approximately 10E8 bacteria were mixed with 0.5 ml of either 0.1M sodium phosphate buffer or S-9 mix, and test substance. The reaction was carried out in triplicate. The mixture was incubated at 37°C for 48 hours, after which time histidine-revertant colonies were counted. The doses selected were separated by half-log intervals. The high dose was 10 mg/plate unless limited by solubility. Positive control chemicals were sodium azide,

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nitro-o-phenylenediamine, 9-aminoacridine and 2-aminoanthracene. Concurrent solvent and positive controls were included in all experiments. A toxicity pretest was conducted to determine the high dose level. This study was conducted with TA 100 in the presence and absence of S-9.

Test substance : 1,2-benzenedicarboxylic acid, dihexyl ester (di-n-hexyl phthalate)

Conclusion : No mutagenic activity was observed at doses up to 10 mg/plate in Salmonella strains TA98, TA100, TA1535 and TA1537 with or without metabolic activation.

Reliability : (1) valid without restriction

Flag : Critical study for SIDS endpoint

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5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

Type : One generation study

Species : mouse

Sex : male/female

Strain : CD-1

Route of admin. : oral feed

Exposure period : Continuous throughout study (beginning 7 days prior to mating).

Frequency of treatm. : Daily throughout pre mating, mating, gestation, and lactation.

Premating exposure period

Male : 7 Days (continuous)

Female : 7 Days (continuous)

Duration of test : 2 generations

No. of generation studies :

Doses : 0.0, 0.3, 0.6, or 1.2% (0, 430, 880, and 1870 mg/kg/day)

Control group : yes

Method : other

Year : 1987

GLP : no data

Test substance : other TS: CAS #84-75-3; 1,2-benzenedicarboxylic acid, dihexyl ester

Method : Control Group: 40 males and 40 females.

Statistical Methods: Cochran-Armitage (dose-related trends); Fisher's exact test (mating and fertility trends); Kruskal-Wallis test and Jonckheere's test (group means for sex ratio); Wilcoxon-Mann-Whitney U test (pairwise comparisons of treatment group means).

Remark : Exposure to DnHP did not affect food consumption but did produce a dose-related decrease in body weight after 13 weeks. There were no litters in the 1.2% group and only 1 pair produced a litter in the 0.6% group compared to all 37 pairs delivering at least one litter in the control group and 14 of 17 pairs in the 0.3% group. The 0.3% group exhibited reduced number of litters per pair, number of live pups/litter, and proportion of live pups. The crossover mating study revealed reduced fertility in both sexes - only 1 of 18 high-dose males sired a litter and none of the high-dose females became pregnant. Sperm assessment of the high-dose males showed that the % motile sperm and sperm concentration were decreased, although the % abnormal sperm was not increased. There were significant decreases in weights of testes, epididymis, and seminal vesicles; atrophy of the seminiferous tubules was observed microscopically. There was a

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	significant decrease (31%) in uterine weight in the female high dose group. Kidney and adrenal weights were decreased, and liver weights increased in both sexes at the high dose although no histopathologic changes were found.
Result	: NOAEL - not determined.
	LOAEL - 0.3% (430 mg/kg/day) for fertility and reproductive endpoints.
Test condition	: There were 40 animals/sex in the untreated control group. Males and females in the treatment groups (20 animals/sex) were exposed to the test substance beginning with a 7-day premating period and throughout a cohabitation period for approximately 14 weeks. Reproductive function was assessed during this cohabitation period for number of litters per pair, number of live pups, sex, live births, and pup weight. These litters were subsequently discarded. Following the 14-week cohabitation, the F0 pairs were separated but continued treatment. Any final litters that were delivered during this time were kept for at least 21 days (weaning). The F0 males and females were necropsied, organs weighed and microscopically examined. Sperm assessment also was performed for the males. A crossover mating trial was then performed to determine whether F0 males or females were more sensitive to adverse effects. High-dose mice of each sex were mated to control mice and the offspring of these crossover matings were examined for litter size, sex, and pup weight. The parents were necropsied.
Test substance	: 1,2-benzenedicarboxylic acid, dihexyl ester (di-n-hexyl phthalate)
Reliability	: (2) valid with restrictions
Flag	: Critical study for SIDS endpoint
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5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	: mouse
Sex	: female
Strain	: CD-1
Route of admin.	: gavage
Exposure period	: Gestation days 6-13
Frequency of treatm.	: Daily
Duration of test	: 7 days
Doses	: 10 ml/kg/day (9900 mg/kg/day)
Control group	: yes, concurrent vehicle
Method	: other
Year	: 1987
GLP	: no data
Test substance	: other TS: CAS #84-75-3; 1,2-benzenedicarboxylic acid, dihexyl ester
Method	: Control Group: 50 females; corn oil only.
	Statistical Methods: ANOVA (maternal body weights at gd6); Fischer's exact test (mortality and number of viable litters); Mann Whitney U-test (maternal body weight gd6 to pd3, number live births, pup survival, pup weight and weight gain).
Result	: NOAEL: Not determined.
	Maternal Effects: One mouse died during the study (1/48). No other maternal effects were reported.
	Embryo/fetal effects: There were no viable litters from 34 confirmed-mated females.
Test condition	: Fifty timed-pregnant female mice were dosed daily on gestation days 6-13 with the test substance. A single dose level of 10 ml/kg was used as the highest practical level due to lack of toxicity (LD10 could not be established). Litters were held until postpartum day 3 then discarded. The

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following data were recorded: maternal observations, survival, and weight gain from gestation day 6 to postpartum day 3; number of live births, number of viable litters, total litter weight, litter weight gain, and pup survival.

Test substance : 1,2-benzenedicarboxylic acid, dihexyl ester (di-n-hexyl phthalate)
Reliability : (2) valid with restrictions
Screening study only; non-standard study design with limited data.
Flag : Critical study for SIDS endpoint
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5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

Type : other: One generation study
In vitro/in vivo :
Species : mouse
Sex : male/female
Strain : CD-1
Route of admin. : oral feed
Exposure period : Continuous throughout study (beginning 7 days prior to mating).
Frequency of treatm. : Daily throughout premating, mating, gestation, and lactation.
Duration of test : 2 generations
Doses : 0.0, 0.3, 0.6, or 1.2% (0, 430, 880, and 1870 mg/kg/day)
Control group : yes
Method : other
Year : 1987
GLP : no data
Test substance : other TS: CAS #84-75-3; 1,2-benzenedicarboxylic acid, dihexyl ester

Method : Control Group: 40 males and 40 females.

Statistical Methods: Cochran-Armitage (dose-related trends); Fisher's exact test (mating and fertility trends); Kruskal-Wallis test and Jonckheere's test (group means for sex ratio); Wilcoxon-Mann-Whitney U test (pairwise comparisons of treatment group means).

Remark : Exposure to DnHP did not affect food consumption but did produce a dose-related decrease in body weight after 13 weeks. There were no litters in the 1.2% group and only 1 pair produced a litter in the 0.6% group compared to all 37 pairs delivering at least one litter in the control group and 14 of 17 pairs in the 0.3% group. The 0.3% group exhibited reduced number of litters per pair, number of live pups/litter, and proportion of live pups. The crossover mating study revealed reduced fertility in both sexes - only 1 of 18 high-dose males sired a litter and none of the high-dose females became pregnant. Sperm assessment of the high-dose males showed that the % motile sperm and sperm concentration were decreased, although the % abnormal sperm was not increased. There were significant decreases in weights of testes, epididymis, and seminal vesicles; atrophy of the seminiferous tubules was observed microscopically. There was a significant decrease (31%) in uterine weight in the female high dose group. Kidney and adrenal weights were decreased, and liver weights increased in both sexes at the high dose although no histopathologic changes were found.

Result : NOAEL - not determined.

LOAEL - 0.3% (430 mg/kg/day) for fertility and reproductive endpoints.

Test condition : There were 40 animals/sex in the untreated control group. Males and females in the treatment groups (20 animals/sex) were exposed to the test substance beginning with a 7-day premating period and throughout a cohabitation period for approximately 14 weeks. Reproductive function was assessed during this cohabitation period for number of litters per pair, number of live pups, sex, live births, and pup weight. These litters were subsequently discarded. Following the 14-week cohabitation, the F0 pairs

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were separated but continued treatment. Any final litters that were delivered during this time were kept for at least 21 days (weaning). The F0 males and females were necropsied, organs weighed and microscopically examined. Sperm assessment also was performed for the males. A crossover mating trial was then performed to determine whether F0 males or females were more sensitive to adverse effects. High-dose mice of each sex were mated to control mice and the offspring of these crossover matings were examined for litter size, sex, and pup weight. The parents were necropsied.

Test substance : 1,2-benzenedicarboxylic acid, dihexyl ester (di-n-hexyl phthalate)
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
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5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

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10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT